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NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Chronic cough due to gastroesophageal reflux in adults: CHEST guideline and Expert Panel report.

Bibliographic Source(s)

Kahrilas PJ, Altman KW, Chang AB, Field SK, Harding SM, Lane AP, Lim K, McGarvey L, Smith J, Irwin RS, CHEST Expert Cough Panel. Chronic cough due to gastroesophageal reflux in adults: CHEST Guideline and Expert Panel report. Chest. 2016 Dec;150(6):1341-60. [51 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Irwin RS. Chronic cough due to gastroesophageal reflux disease: ACCP evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):80S-94S. [89 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The grades of recommendation (1A–2C, consensus-based [CB]) and the approach to rating the quality of evidence are defined at the end of the "Major Recommendations" field.

1. In adult patients with chronic cough, the Expert Panel suggests that the cough be managed according to a published management guideline that initially considers the most common potential etiologies as well as symptomatic gastroesophageal reï¬‚ux (ungraded, consensus based).
   Remarks: Common potential etiologies include environmental or occupational irritants, primary or secondary smoking, use of angiotensin-converting-enzyme (ACE) inhibitors, abnormal chest radiographic ï¬ndings, asthma, upper airway cough syndrome due to a variety of rhinosinus conditions, nonasthmatic eosinophilic bronchitis, and suppurative lung disease. Often, more than one etiology is a contributing factor.

2. In adult patients with chronic cough suspected to be due to reï¬‚ux-cough syndrome, the Expert Panel recommends that treatment include (1) diet modiï¬cation to promote weight loss in overweight or obese patients; (2) head of bed elevation and avoiding meals within 3 hours of bedtime; and (3) in patients who report heartburn and regurgitation, proton pump inhibitors (PPIs), H_2-receptor antagonists, alginate, or antacid therapy sufï¬cient to control these symptoms (Grade 1C).
   Remarks: (1) While it is expected that gastrointestinal (GI) symptoms will respond within 4-8 weeks, the literature suggests that improvement in cough may take up to 3 months. (2) Head of bed elevation is suggested based on its utility for improving GI

gastroesophageal reflux disease (GERD) symptoms while acknowledging that it has not been demonstrated to be beneï¬cial for cough.

3. In adult patients with suspected chronic cough due to reï¬‚ux-cough syndrome, but without heartburn or regurgitation, the Expert Panel recommends against using PPI therapy alone because it is unlikely to be effective in resolving the cough (Grade 1C).
4. In adult patients with chronic cough potentially due to reï¬‚ux-cough syndrome who are refractory to a 3-month trial of medical antireï¬‚ux therapy and are being evaluated for surgical management (antireï¬‚ux or bariatric), or in whom there is strong clinical suspicion warranting diagnostic testing for gastroesophageal reï¬‚ux, the Expert Panel suggests that they undergo esophageal manometry and pH-metry with conventional methodology (Grade 2C).
   Remarks: Esophageal manometry is done both to evaluate for a major motility disorder and to accurately position the pH electrode for the pH monitoring study. With conventional methodology, the pH electrode is placed 5 cm proximal to the lower esophageal sphincter, and the study is done off antisecretory medications after withholding PPI therapy for 7 days and H_2 receptor antagonists for 3 days prior to the study. It was agreed by consensus of the Esophageal Diagnostic Advisory Panel composed of both gastroenterologists and surgeons that this is the only methodology with proven validity with respect to surgical outcomes.

5. In adult patients with chronic cough and a major motility disorder (e.g., absent peristalsis, achalasia, distal esophageal spasm, hypercontractility) and/or normal acid exposure time in the distal esophagus, the Expert Panel suggests not advising antireï¬‚ux surgery (Grade 2C).
   Remarks: Under the circumstances of a major motility disorder or normal esophageal acid exposure on esophageal pH-metry, there is no supportive controlled data for antireï¬‚ux surgery and there is quantiï¬able risk to the procedure making for an unacceptable risk-beneï¬t ratio.

6. In adult patients with chronic cough, adequate peristalsis, and abnormal esophageal acid exposure determined by pH-metry in whom medical therapy has failed the Expert Panel suggests antireï¬‚ux (or bariatric when appropriate) surgery for presumed reï¬‚ux-cough syndrome (Grade 2C).
   Remarks: With respect to deï¬ning adequate peristalsis, there is no consensus. Some consider any preserved peristalsis to be adequate while others stipulate that it must be at least 30% and others at least 50% of normal.

Definitions

American College of Chest Physicians (CHEST) Grading System

Grade of Recommendation	Balance of Benefit vs. Risk and Burdens (Strength of the Recommendation: Level 1 or 2)	Methodologic Strength of Supporting Evidence (Quality of Body of Evidence: A, B, C, or CB)	Implications
Graded evidence-based guideline recommendations			
Strong recommendation, high-quality evidence (1A)	Benefits clearly outweigh risk and burdens or vice versa	Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect.
Strong recommendation, moderate-quality evidence (1B)	Benefits clearly outweigh risk and burdens or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate.
Strong recommendation, low- or very-low-quality evidence (1C)	Benefits clearly outweigh risk and burdens or vice versa	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate.
Weak recommendation, high-quality evidence (2A)	Benefits closely balanced with risks and burden	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the estimate of effect.
Weak	Benefits closely	Evidence from RCTs with important	Best action may differ depending on

Grade of Recommendation	Balance of Benefit vs. Risk and Burdens (Strength of the Recommendation: Level 1 or 2)	Methodologic Strength of Supporting Evidence (Quality of Body of Evidence: A, B, C, or CB)	Implications
recommendation, moderate-quality evidence (2B)	balanced with risks and burden	limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies	circumstances or patient's or societal values. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate.
Weak recommendation, low- or very-low-quality evidence (2C)	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Evidence for at least one critical outcome from observational studies, case series, or RCTs, with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate.
Nongraded consensus-based suggestions			
Consensus-based (CB)	Uncertainty due to lack of evidence but expert opinion that benefits outweigh risk and burdens or vice versa	Insufficient evidence for a graded recommendation	Future research may well have an important impact on confidence in the estimate of effect and may change the estimate.

Clinical Algorithm(s)

None available

Scope

Disease/Condition(s)

Chronic cough due to gastroesophageal reflux disease (GERD)

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Gastroenterology

Internal Medicine

Pulmonary Medicine

Intended Users

Physicians

Guideline Objective(s)

To update the 2006 American College of Chest Physicians clinical practice guidelines for the diagnosis and treatment of chronic cough due to reï¬‚ux using an evidence-based approach

Target Population

Adult patients with more than an 8-week history of refractory chronic cough

Interventions and Practices Considered

1. Management of cough that considers most common potential etiologies, as well as symptomatic gastroesophageal reflux
2. Treatment that includes the following for adult patients with chronic cough suspected to be due to reflux-cough syndrome
    - Diet modification in overweight or obese patients
    - Head of bed elevation and avoiding meals within 3 hours of bedtime
    - Proton pump inhibitors (PPIs), H_2-receptor antagonists, alginate, or antacid therapy in patients who report heartburn and regurgitation
3. Esophageal manometry and pH-metry with conventional method
4. Antireflux (or bariatric when appropriate) surgery for presumed reflux-cough syndrome

Note: The following interventions were considered but not recommended:

- PPI therapy alone in adult patients with suspected chronic cough due to reflux-cough syndrome, but without heartburn or regurgitation
- Advising antireflux surgery in adult patients with chronic cough and a major motility disorder and/or normal acid exposure time in the distal esophagus

Major Outcomes Considered

- Differential reduction or remission of chronic cough according to whether or not the designated interventions were rendered
- Differential reduction or remission of chronic cough with therapy directed at gastroesophageal reflux according to whether or not patients with chronic cough meet the designated "minimal clinical criteria"

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search

The methods used for this systematic review conformed to those outlined in the article "Methodologies for the Development of American College of Chest Physicians (CHEST) Guidelines and Expert Panel Reports" (see the "Availability of Companion Documents" field). Systematic reviews and clinical trials were identiï¬‚ed from searches of electronic databases (Ovid Medline, and EMBASE) commencing from the earliest available date until May 2015. A search of the Cochrane database returned 82 articles, eight of which were suffï¬‚ciently relevant for full text review; however, none met criteria for inclusion in this review. The reference lists of retrieved articles were examined for additional citations. The search terms used were ("Gastroesophageal Reï¬‚ux" [MeSH] OR GERD OR GORD OR reï¬‚ux OR gastroesophageal reï¬‚ux disease OR reï¬‚ux esophagitis OR nonerosive reï¬‚ux disease OR NERD) AND ("Proton Pump Inhibitors" [MeSH] OR PPI OR omeprazole OR lansoprazole OR pantoprazole OR rabeprazole OR esomeprazole OR tenatoprazole OR "Histamine H2 Antagonists" [MeSH] OR prokinetic OR surgery) AND cough. The titles and abstracts of the search results were independently evaluated by two reviewers to identify potentially relevant articles. The full texts of all potentially relevant articles were retrieved, and two reviewers independently reviewed all retrieved studies. A third reviewer was

available to adjudicate any disagreements.

Number of Source Documents

The results of the literature search for the first question appear in Figure 1 in the original guideline document. The search initially identified 1,870 citations. After the removal of 354 duplicates, 1,516 records were screened, with 541 being excluded on the basis of irrelevant titles and 119 on the basis of being relevant to pediatrics. Hence, 842 abstracts were reviewed. Among these, 14 were controlled medical trials potentially pertinent to PICO question #1. The results of the search for the second question appear in Figure 2 in the original guideline document. Initial searching identified 1,877 records. After the removal of 354 duplicates, 1,523 records were screened, with 541 being excluded on the basis of irrelevant titles and 119 on the basis of being relevant to pediatrics. Hence, 849 abstracts were reviewed. Among these, 14 full-text articles were assessed for eligibility and deemed pertinent for qualitative synthesis for inclusion. The additional seven studies for PICO question 2 were identified in the recent publication on intervention fidelity.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Based on the Grades of Recommendations Assessment, Development and Evaluation (GRADE) approach, quality of evidence (also known as certainty of evidence) is defined as the extent to which confidence in the effect estimate is adequate to support a recommendation. The quality of evidence is categorized as high (A level), moderate (B level), or low (includes very low) (C level). The rating of the quality of evidence reflects the strengths and limitations of the body of evidence and was based on the study design, risk of bias, imprecision, inconsistency, indirectness of results, and likelihood of publication bias, in addition to factors specific to observational studies (see the "Rating Scheme for the Strength of the Recommendations" field).

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Quality Assessment

Included articles underwent methodological assessment. For the randomized controlled trials (RCTs), quality assessment was carried out with the Cochrane Risk of Bias Tool if the following criteria were met: (1) study excluded other common causes of chronic cough (asthma, upper airway cough syndrome [UACS]) by adequate workup *and* (2) included patients both with and without additional symptoms of gastroesophageal reflux disease (GERD) or laryngopharyngeal reï¬,ux (LPR), or both, *or* included patients with and without additional test results suggestive of GERD or LPR, or both. For observational studies, quality assessment was done with the Cochrane Risk of Bias Tool for cohort studies.

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

The Expert Panel used the published methodology of the American College of Chest Physicians (CHEST) Guideline Oversight Committee to

select the Expert Cough Panel Chair and the International Panel of Experts to perform a systematic review and synthesis of evidence and to develop recommendations and practice management suggestions. After generating the key clinical questions for this systematic review, population, intervention, comparison, outcome (PICO) elements were derived to inform the literature review. The questions were formulated after polling the existing writing group for key clinical questions related to chronic cough due to gastroesophageal reflux disease (GERD). This returned a list of 20 questions that were then synthesized into two PICO questions that were sufficiently broad to capture most of the detail from those 20 questions. The resultant PICO questions that formed the basis of the subsequent systematic review are stated in Table 2 in the original guideline document.

The questions that formed the basis of the systematic review were the following: (1) Can therapy intended to treat gastroesophageal reflux improve or eliminate cough in adults with refractory chronic cough? (2) Are there minimal clinical criteria to guide clinical practice in determining that a patient's chronic cough is likely to respond to therapy for gastroesophageal reflux?

The findings of the systematic review were used to support the evidence-graded recommendations or suggestions. A structured consensus-based Delphi approach was used to provide expert advice on guidance statements. In this regard, for a recommendation or suggestion to be approved by the Expert Cough Panel, 75% of the eligible panel members had to vote, and 80% of those voting had to strongly agree or agree with the statement. Quality assessment also included grading the strength of recommendations based on consideration of the balance of benefits to harms, patient values and preferences, and the quality of the evidence supporting the recommendation. Harms incorporated risks and burdens to the patients that can include convenience or lack of convenience, difficulty of administration, and invasiveness.

Rating Scheme for the Strength of the Recommendations

American College of Chest Physicians (CHEST) Grading System

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Strong recommendation, low- or very-low-quality evidence (1C)	Benefits clearly outweigh risk and burdens or vice versa	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate.
Weak recommendation, high-quality evidence (2A)	Benefits closely balanced with risks and burden	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the estimate of effect.
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(2C)	burden may be closely balanced		
Nongraded consensus-based suggestions			
Consensus-based (CB)	Uncertain about balance of evidence but expert opinion that benefits outweigh risk and burdens or vice versa	Insufficient evidence for a graded recommendation	Future research may well have an important impact on confidence in the estimate of effect and may change the estimate.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Improvement or elimination of cough due to gastroesophageal reflux disease

Potential Harms

Harms incorporated risks and burdens to the patients that can include convenience or lack of convenience, difficulty of administration, and invasiveness.

Qualifying Statements

Qualifying Statements

American College of Chest Physicians (CHEST) guidelines are intended for general information only, are not medical advice, and do not replace professional medical care and physician advice, which always should be sought for any medical condition. The complete disclaimer for this guideline can be accessed at http://www.chestnet.org/Guidelines-and-Resources/Guidelines-and-Consensus-Statements/CHEST-Guidelines .

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Kahrilas PJ, Altman KW, Chang AB, Field SK, Harding SM, Lane AP, Lim K, McGarvey L, Smith J, Irwin RS, CHEST Expert Cough Panel. Chronic cough due to gastroesophageal reflux in adults: CHEST Guideline and Expert Panel report. Chest. 2016 Dec;150(6):1341-60. [51 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Dec

Guideline Developer(s)

American College of Chest Physicians - Medical Specialty Society

Source(s) of Funding

The American College of Chest Physicians (CHEST) was the sole supporter of these guidelines, this article, and the innovations addressed within.

Guideline Committee

American College of Chest Physicians (CHEST) Expert Cough Panel

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Financial Disclosures/Conflicts of Interest

The authors have reported to *CHEST* the following: P. J. K., K. W. A., S. K. F., S. M. H., A. P. L., K. L., and L. M. report no financial or intellectual conflicts of interest pertinent to either population, intervention, comparison, outcome (PICO) question #1 or #2. A. B. C. reports an intellectual conflict of interest pertinent to PICO question #1 as it assesses one paper that she authored; she reports no financial conflict of interest pertinent to either PICO question #1 or #2. J. S. is a named inventor on a patent that describes novel techniques for detecting cough from sound recordings pertinent to PICO question #2. This patent is owned by the University Hospital of South Manchester and is licensed to a medical device company. She reports no financial conflict of interest pertinent to either PICO question #1 or #2. R. S. I. discloses that he has no financial or intellectual conflicts of interest pertinent to either PICO question #1 or #2. Moreover, although R. S. I. is the Editor in Chief of *CHEST*, the review and all editorial decisions regarding this manuscript were made independently by others.

Guideline Endorser(s)

American Academy of Otolaryngology - Head and Neck Surgery Foundation - Medical Specialty Society

American Association for Respiratory Care - Professional Association

American College of Allergy, Asthma and Immunology - Medical Specialty Society

Asian Pacific Society of Respirology - Disease Specific Society

Canadian Thoracic Society - Medical Specialty Society

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This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the CHEST Journal Web site . Also available to CHEST Journal subscribers through the CHEST app for iPhone, iPad, and iPod Touch.

Availability of Companion Documents

The following is available:

- Lewis SZ, Diekemper RL, Ornelas J, Casey KR. Methodologies for the development of CHEST guidelines and Expert Panel reports. Chest. 2014 Jul;146(1):182-92. Available from the CHEST Journal Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on May 4, 2006. The information was verified by the guideline developer on June 5, 2006. This summary was updated by ECRI Institute on July 26, 2010 following the U.S. Food and Drug Administration (FDA) advisory on Proton Pump Inhibitors (PPI). This summary was updated by ECRI Institute on March 3, 2017.

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